Hepatitis C: The Cure

Patrick Marcellin
Who you are
1100 participants from 70 countries
Hepatitis C
Where we are:
The achievements
Hepatitis C: progress is accelerating

The conclusion of the PHC 2009

- Cure = 100% in 10 years
Progress is accelerating

Earlier?

2015?
Where we are
Better understanding of therapeutic targets

Protease Inhibitors
NS5A Inhibitors
Polymerase Inhibitors
Where we are
Better efficacy with triple therapy (G1)

- 2002 BI
  - 40%
- 2012 TRI
  - 70%
  - +30%

Jacobson et al. NEJM 2012
Poordad NEJM 2012
SVR = CURE

- Undetectable HCV RNA in serum: 100%
- Undetectable HCV RNA in liver: $\approx 100\%$
- Undetectable HCV RNA in PBMCs: 100%
Cure = improved prognosis

HCC in 300 cirrhotics

Time since last treatment (years)

SVR (+)

SVR (-)

p < 0.001

Cardoso et al. J Hepatol 2010
Cure = improved prognosis

Survival in 300 cirrhotics

Time since last treatment (years)

SVR (+)

SVR (-)

p < 0.001

Cardoso et al. J Hepatol 2010
Reinforced screening and access to therapy = decrease in HCV-related mortality

Percentage of decreased mortality (genotype 1) modelisation 2012 – 2021 France

- PEG-IFN + RBV
- Tritherapy PEG IFN + RBV + PI
- Tritherapy + reinforced screening + improved access to therapy

Deuffic-Durban et al. EASL 2011
Where we are:
the limitations
Where we are: limitations

Insufficient screening

- **Undiagnosed Pool**
  - USA: 2.5 million
  - EU: 1.8 million

- **Diagnosed Pool**
  - USA: 0.9 million
  - EU: 1.6 million
Where we are: limitations

170 million people HCV infected worldwide

- US 4M
- Brazil 7M
- Europa 5M
- Russia 3M
- Egypt 12M
- Pakistan 9M
- India 10M
- Vietnam 7M
- China 43M
- Korea 1M
- Japan 2M

170 million people HCV infected worldwide
Where we are: limitations

Insufficient access to treatment
Where we are: limitations

Access to treatment: the bottle necks

- Diagnosed
- Managed
- Treated
- Cured
Where we are: limitations

No efficacy of triple therapy in G non 1

- 2002 BI: 50-80%
- 2013 TRI: 50-80%
Where we are: limitations

High prevalence of G non1 in high prevalence countries
Where we are:
The hope
Ideal Therapy

- 100% efficacy
- IFN-free
- All oral
- Short duration
- No resistance
- Pan-genotypic
- Well tolerated and safe
- Low cost
Quadruple therapy: PEG-IFN + RBV + NS5AI + PI in G1 null responders: IFN free
Danoprevir + mericitabine + ribavirine in non-responders G1

SVR 12

Partial Responders: 9/23 (39%)
Null Responders: 17/31 (55%)

Feld JJ, AASLD 2012
Faldaprevir + BI 207127 + RBV (naive G1)


Patients with HCV RNA <25 IU/mL (%)

<table>
<thead>
<tr>
<th></th>
<th>400 mg TID BI 207127 + BI 201335 + RBV</th>
<th>600 mg TID BI 207127 + BI 201335 + RBV</th>
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</thead>
<tbody>
<tr>
<td>Day 15</td>
<td>6/15 (40%)</td>
<td>14/17 (82%)</td>
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<tr>
<td>Day 22</td>
<td>10/15 (67%)</td>
<td>17/17 (100%)</td>
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<tr>
<td>Day 29</td>
<td>11/15 (73%)</td>
<td>17/17 (100%)</td>
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ABT-450/r + ABT-333 + ABT-267 + RBV

SVR 12 (ITT)

8W Naïve patient: 87%
12W Naïve Patients: 98%
12W Null Responders: 93%

Kowdley et al. AASLD 2012
Sofosbuvir (GS 7977) + GS 5885 + RBV

HCV RNA < 15 UI/ml

- Naive: SOF + RBV (88)
- Null responders: SOF + RBV (10)
- Naive: SOF + GS-5885 + RBV (100)
- Null responders: SOF + GS-5885 + RBV (100)

Gane et al. AASLD 2012
The Proof of Concept

- 100% efficacy
- All oral
- IFN-free
- Short duration
- No resistance
- Pan-genotypic

- Well tolerated and safe
- Low cost
ORGANIZING COMMITTEE:

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NATHALIE BOYER
OLIVIER LADA
MICHELLE MARTINOT
FACULTY
# IFN-free ongoing trials: summary

<table>
<thead>
<tr>
<th>First drug (company)</th>
<th>Second drug</th>
<th>Third drug</th>
<th>Fourth drug</th>
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<tr>
<td><strong>Boehringer ingelheim</strong></td>
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<td>Faldaprevir (BI201335)</td>
<td>BI207127</td>
<td>Ribavirin</td>
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<td>Protease inhibitor</td>
<td>NS5B NNI</td>
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<td><strong>Abbott</strong></td>
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<td>ABT 333</td>
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<td>ABT-450/r Protease inhibitor</td>
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<td><strong>Gilead/BMS</strong></td>
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<td>Sofosbuvir (GS 7977)</td>
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<td><strong>Vertex</strong></td>
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<tr>
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<td>NS5B</td>
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Impact of treatment on mortality

incidence annuelle de la mortalité liée au VHC

Without treatment

With bitherapy PEG IFN + RBV

-14%

G1/4

-32%

G2/3

Deuffic-Durban et al. J Hepatol 2007
Reinforced screening and access to therapy = decrease in HCV-related mortality

Percentage of decreased mortality (genotype 1) modelisation 2012 – 2021 France

- PEG-IFN + RBV
- Tritherapy PEG IFN + RBV + PI (+ 19 %)
- Tritherapy + reinforced screening + improved access to therapy (+ 83 %)

Deuffic-Durban et al. EASL 2011
Where we go
Where we go